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Research Progress of Chinese and Western Medicine Treatment for Diarrheal Irritable Bowel Syndrome

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Abstract: *Irritable bowel syndrome with diarrhea (IBS-D) is one of the subtypes of irritable bowel syndrome (IBS), which is a common gastrointestinal disease characterized by disorder of brain-gut axis interaction. Clinical manifestations encompass abdominal distension, abdominal pain, as well as alterations in defecation pattern and frequency. IBS exhibits a protracted duration and frequent relapses, significantly compromising the overall well-being and psychological state of the majority of patients. At present, it is believed that the disease has a variety of pathogenic factors and a complex pathological mechanism. The current clinical guidelines for the diagnosis and management of IBS primarily focus on symptomatic relief, while traditional Chinese medicine offers distinctive advantages in IBS addressing. This article reviews the traditional Chinese medicine and western medicine in the treatment of IBS-D, encompassing both pharmacological and non-pharmacological interventions. The aim is to provide valuable insights for clinicians seeking evidence-based approaches for treating this condition.*

Keywords: *Diarrhea-predominant irritable bowel syndrome; Clinical treatment; Traditional Chinese Medicine*

1. Introduction

IBS is a prevalent chronic functional bowel disorder that arises from disrupted intestinal-brain interactions and manifests as recurrent abdominal distension or pain, changes in defecating frequency or character [1]. It can be classified into four subtypes [2]: diarrhea-predominant IBS (IBS-D), constipation-predominant IBS (IBS-C), mixed-predominant IBS (IBS-M) and unspecified IBS (IBS-U). According to a cross-sectional survey conducted by the Rome Foundation, the pooled prevalence of IBS ranges between 1.3% and 7.6%, with an overall prevalence of 4.1% [3,4]. In China, the overall prevalence of IBS in the general population is 1.4%-11.5%, while the prevalence of IBS is as high as 10.7%-34.3% in gastroenterology clinics, and it is slightly higher in women than in men [5,6]. IBS-D was the most common subtype, accounting for 31.5% of IBS patients [7]. Because the Rome IV criteria for diagnosing IBS were more stringent than its predecessor, the Rome III criteria, by deleting the term "abdominal discomfort," the frequency of symptoms required for abdominal pain increased from at least 3 days per month to at least 1 day per week [8]. As a result, many patients previously diagnosed with IBS will now be classified as having other functional bowel disorders, and the disease implications for the patient are also substantial [7], as shown in Table 1. IBS is a chronic and long-term disease. Although it does not pose a life threat, it has a significant impact on the quality of life of patients. IBS patients are often accompanied by psychological comorbidities such as anxiety and depression. The lack of definitive physical and chemical diagnostic criteria for IBS, coupled with the absence of a consensus on its underlying pathophysiological mechanism, poses challenges in establishing a unified understanding. The current understanding suggests that the etiology of this condition involves a complex interplay of various factors, including interactive brain abnormalities. Potential risk factors encompass genetic predisposition, dietary influences, gastrointestinal disorders, visceral hypersensitivity, gastrointestinal tract infections, and psychological factors. Importantly, these factors can exert bidirectional effects on the brain-gut axis [8,9], as shown in Figure 1. In recent years, the management of IBS-D has become increasingly diverse, leading to various controversies surrounding existing pharmacological and non-pharmacological interventions. The role of traditional Chinese medicine in the treatment of IBS-D has also garnered growing attention both domestically and internationally.

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Table 1: Differences in the prevalence of irritable bowel syndrome between Roman IV diagnosis and Roman III diagnosis

FGID	Overall	Sex		Age group (years)		
		Females	Males	18-39	40-64	65+
Internet						
Rome IV IBS	3.8 (3.6, 4.0)	4.8 (4.4, 5.1)	2.9 (2.6, 3.1)	4.9 (4.5, 5.3)	3.3 (3.0, 3.6)	1.9 (1.6, 2.3)
Rome III IBS	10.1 (9.8, 10.5)	12.6 (12.1, 13.2)	7.8 (7.3, 8.2)	11.5 (11.0, 12.1)	9.7 (9.1, 10.2)	7.5 (6.78, 8.2)
Report						
Rome IV IBS	1.5 (1.3, 1.7)	2.0 (1.7, 2.3)	1.0 (0.8, 1.2)	1.4 (1.1, 1.7)	1.5 (1.2, 1.7)	1.9 (1.4, 2.4)
Rome III IBS	3.5 (3.3, 3.81)	4.1 (3.7, 4.5)	3.0 (2.6, 3.3)	2.9 (2.5, 3.2)	3.4 (3.0, 3.8)	5.5 (4.7, 6.3)

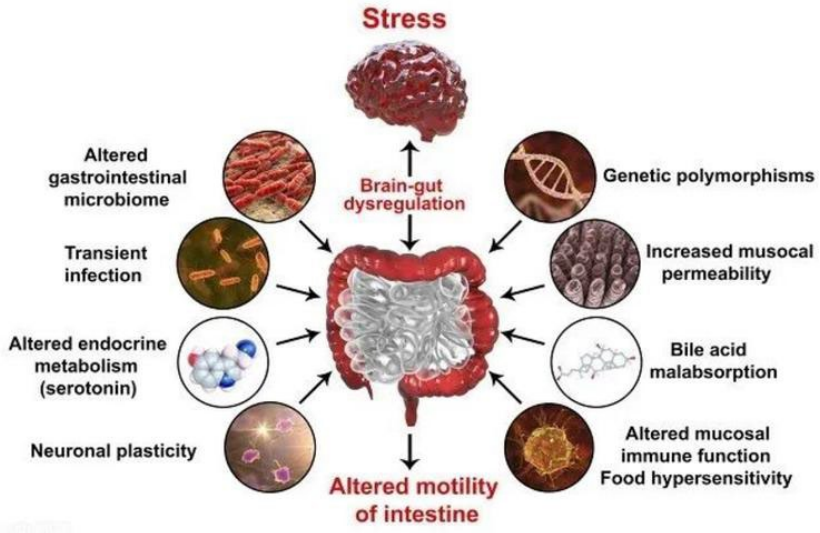

Figure 1: Brain-gut axis

2. TCM's comprehension of IBS-D

IBS-D belongs to the modern medical disease name, according to its clinical manifestations, traditional Chinese medicine (TCM) classifies it as "diarrhea," "constipation," "abdominal pain," and "depression syndrome." Modern physicians believe that factors such as physical susceptibility, exposure to external pathogens, improper diet, emotional disorders, visceral dysfunctions, and phlegm-dampness stasis are associated with the development of IBS-D [10]. Lin Yangjin et al. [11] categorized IBS-D patients based on the TCM Physique Classification and Judgment national standard. Utilizing descriptive statistical methods, it was determined that individuals with damp-heat and liver-qi stagnation exhibited the highest susceptibility to IBS-D. Most were men with damp-heat and women with liver-qi stagnation. The allergic constitution caused by food intolerance or allergy is related to the occurrence of IBS-D, supporting the theory of corporeity [12]. The physicians of previous dynasties also coined phrases like "no dampness, no diarrhea" and "increased dampness leads to five discharges," which exemplified the theory of exogenous infection. The presence of cold pathogens and dampness in the large intestine leads to constriction of the intestinal organs and meridians, resulting in impaired flow of qi and blood as well as disrupted intestinal peristalsis. Symptoms may include abdominal pain and clear or watery diarrhea. Additionally, heat and damp fumigation of the large intestine can also disrupt intestinal peristalsis, leading to urgent or difficult bowel movements accompanied by abdominal pain and anal burning sensation. The theory of "Zangfu rheumatism" of Professor Tong Hsiaolin [13] also highlights the significance of diarrhea resulting from dampness. Improper diet will hurt the spleen, such as eating raw and cold, spicy food, greasy, sweet and delicate food or food with strong taste, leading to spleen and stomach dysfunction, intestinal fluid absorption disorders and diarrhea. 10 In China, scholars suggest consuming invigorating and diuretic foods to promote spleen function, eliminate dampness, and provide

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antiviral effects [14]. Western countries have proposed a low FODMAP diet [15]. In terms of the pathogenesis of emotional disorders, it was acknowledged as early as in Huangdi Neijing that emotions are intricately linked to individuals' inherent constitution. During the Ming Dynasty, Zhang Jiebin, a renowned physician, authored an article titled "Nine Qi of Emotions" to elucidate the correlation between emotions and diseases. Emotional disorders can cause qi imbalances, resulting in pain and fullness. Prolonged disruption of qi regulation may lead to visible symptoms like blood stasis and phlegm accumulation. The bidirectional regulation between the central nervous system (CNS) and enteric nervous system has been demonstrated, highlighting the significance of psychological comorbidity within the bio-psycho-social model. This aspect holds crucial importance in investigating the etiology of IBS [9]. Imbalance of energy leads to pathogenic factors, causing organ dysfunction and increased disease susceptibility. Huangdi Neijing suggests that the regulation of gas flow in the five zang-organs and anal opening and closing has an impact on normal viscera qi activity, thereby closely influencing the shape, quality, and frequency of stool. Therefore, the dysfunction of the viscera is therefore a significant pathogenic factor in IBS-D [10]. Pathological manifestations in Chinese medicine theory include phlegm, dampness, and blood stasis. These factors worsen organ dysfunction and create a harmful cycle. Traditional Chinese medicine treats IBS-D by strengthening the spleen, eliminating excess water and dampness, improving blood circulation to resolve stasis, and promoting optimal flow of qi and blood through unblocking meridians.

3. Internal therapy

3.1. TCM Prescription

Chinese expert consensus of irritable bowel syndrome in 2020 5 relates to the TCM prescription for the treatment of IBS-D as shown in Table 2.

Table 2: Dialectical classification of IBS-D and treatment with classical prescriptions

Types	Prescriptions	Herbal medicine composition
liver-depression and spleen-deficiency syndrome	Tongxieyaofang formula	Rhizoma Atractylodis Macrocephalae, Radix paeoniae alba, Radix sileris, Pericarpium citri reticulatae
Spleen deficiency and dampness excess syndrome	shenlingbaizhu powder	Pulp of lotus seed,semen coicis,Fructus Amomi,Platycodon grandiflorum,White Hyacinth Bean,Poria cocos, Panax ginseng, Glycyrrhiza, Rhizoma Atractylodis Macrocephalae, Common Yam Rhizome
the yang deficiency of spleen and kidney	aconitum lizhong pill combined with sishen pill	Radix Aconite Lateralis Preparata, Panax ginseng, Dried ginger, Glycyrrhiza, Rhizoma Atractylodis Macrocephalae, Fructus Psoraleae, Myristica fragrans, Medcinal Evodia Fruit, Schisandra chinensis
spleen-stomach damp-heat syndrome	Gegen Huangqin Huanglian Decoction	Pueraria Lobata, Glycyrrhiza, Radix Scutellariae, Coptis chinensis
syndrome of intermingled heat and cold	wumei pills	Dark Plum Fruit, Asarum,Dried ginger, Coptis chinensis, Radix Aconite Lateralis Preparata, Chinese angelica, Phellodendron amurense, Cassia twig,Panax ginseng, Chinese prickly ash

The most prevalent syndrome associated with IBS-D is characterized by liver stagnation and spleen deficiency. Tongxie Yaofang, a traditional Chinese medicine prescription, is widely used to address the symptoms of pain and diarrhea caused by liver stagnation and spleen deficiency. It functions by invigorating the spleen, soothing the liver, eliminating dampness, and alleviating diarrhea. The findings of several studies have demonstrated that Tongxie Yaofang can modulate the balance of brain-enteric nervous system and gut-brain peptide, thereby reducing internal hypersensitivity, alleviating intestinal inflammation, regulating intestinal immunity, and promoting restoration of the mucous membrane barrier [16]. It may be involved in the regulation of serotonin 5-hydroxytryptamine signaling pathway and activation of p38 mitogen-activated protein kinase (MAPK) signaling pathway [17], inhibition of abnormal activation of NF-κB and Notch signaling pathways [18], regulating the balance between Th17 and Treg immune responses, which are the two polarization directions of CD+4 in intestinal immune

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cells [19]. And the Vasoactive intestinal peptide (VIP) pathway modulates the PKA-cAMP pathway to downregulate the expression of Aquaporin-8 (AQP8) [6]. According to the basic prescriptions of clinical patients, modern doctors have evolved modified Tongxie yaofang [20], Tongxie Sishen Soup [21], Tongxie Anpi decoction [22], and etc. A plethora of studies have demonstrated that traditional Chinese medicine compounds possess the advantages of being multi-component, multi-targeted, and multi-pathway in the treatment of IBS-D, thereby exhibiting a favorable therapeutic effect on this condition.

3.2. TCM monomer

The radix sileris possesses the functions of heat-clearing and detoxification, surface-wind removal, dampness dispelling, and pain relief. The wind extract contains polysaccharides, organic acids, volatile oil, chromogenone, and other components. It exhibits various pharmacological activities such as anti-inflammatory, antibacterial, antioxidant, antipyretic, and analgesic effects [23]. The rhizoma atractylodis has dampness-drying and spleen-strengthening properties, as well as wind-eliminating and cold-dispersing effects. Atractylodis atractylodis, found in the volatile oil derived from it, has anti-inflammatory, analgesic, anti-ulcer activities and regulates gastrointestinal motility [24]. Alhagi, a herb used in Xinjiang ethnic medicine, can treat abdominal pain, distention, diarrhea, and other gastrointestinal issues. Research shows it regulates gut movement and sensitivity [25]. Patchouli fragrance is pungent and mild, and it can aromatize moisture, alleviate heat, and suppress vomiting. Patchouli alcohol is the main component in patchouli essential oil. Studies have shown that patchouli formula granules can improve visceral hypersensitivity and defecation in IBS-D rats by down-regulating a non-coding gene associated with 5-hydroxytryptamine receptor expression [26]. The main constituent of Rhizoma coptidis is berberine (BBR). Extensive research has demonstrated that BBR possesses potent anti-inflammatory, antibacterial, analgesic, and antidiarrheal properties along with a diverse range of biological activities [27]. LI et al. [28] revealed that a natural self-assembly of BBR and baicalin (BA) occurs, resulting in the formation of BA-BBR nanoparticles (BA-BBR NPs). These BA-BBR NPs reduced 5-HT levels in colon tissue and serum, improving visceral hypersensitivity and alleviating IBS-D symptoms. Aconitum medicine promotes qi circulation, relieves pain, warms the kidneys, and dispels coldness. Modern pharmacology studies found that Linderae Radix water extract (LRWE) can modulate 25 potential biomarkers related to metabolism in serum. It also enhances intestinal barrier function, improves immune response, and reduces discomfort, diarrhea, and inflammation in the intestines [29]. The radix paeoniae alba has yang-warming, dampness-dispelling, deficiency-supplementing, and spleen-stomach-invigorating effects. Its total glucosides are the active constituents in Chinese herb Paeoniae alba. Sun Yanning et al. [30] suggests that radix paeoniae alba total glycosides can alleviate diarrhea symptoms in IBS-D rats by regulating the serotonin signal pathway and reducing intestinal sensitivity.

4. External Therapy

The external treatment of traditional Chinese medicine has extensive prospects for clinical application due to its low operational difficulty, minimal side effects, and lower recurrence rate [31]. In the treatment of IBS, acupuncture offers multi-faceted action, bidirectional benign interaction, and saturation regulation to achieve internal disease and external treatment effects [32]. The use of Chinese medicine enema has been prevalent for treating intestinal disorders since ancient times, with relevant documentation dating back to Zhang Zhongjing's Shang Han Lun during the Han Dynasty. The enema therapy for IBS-D allows direct drug delivery to the affected site, maximizing its therapeutic effect. Transrectal administration achieves higher drug concentration at the lesion site and exhibits enhanced efficacy due to the rich venous plexus in the rectum and robust blood circulation. It offers superior utilization rate and faster onset of action compared to oral medication. The massage technique, documented in the Huangdi Neijing, targets specific acupoints and meridians to invigorate the spleen and regulate qi and blood flow. Counterclockwise abdominal pushing and rubbing show significant efficacy in strengthening the spleen, alleviating diarrhea symptoms, promoting Yang energy, and benefiting qi circulation in patients with functional diarrhea. Additionally, massage therapy has excellent patient compliance, high safety standards, and reliable therapeutic outcomes compared to drug treatments. The stimulation of auricular points through techniques like sticking and electroacupuncture offers a non-invasive and minimally discomforting approach to prevent and treat diseases.

5. Summary

So far, the clinical management of IBS-D has primarily focused on pharmacotherapy, yet there is a

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lack of unitive clinical guidelines. TCM not only circumvent the adverse reactions associated with Western medicine treatment but also effectively alleviate gastrointestinal symptoms in patients with IBS-D, improve negative emotions, and enhance their quality of life. As an alternative or adjunctive approach to Western medicine treatment, it holds significant value in clinical applications. Although TCM partially compensate for the limitations of Western medicine treatment, a standardized treatment plan has not been established as yet. Clinical management necessitates physicians to develop personalized treatment plans based on individual patient circumstances. Furthermore, despite achieving certain outcomes in intervening IBS-D through TCM. There remains a dearth of high-quality clinical evidence and implementation strategies. Therefore, conducting systematic and comprehensive research into TCM for IBS-D bears great clinical significance.

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